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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,943	04/20/2005	Ayrookaran J. Poulse	GC716-2-US	1170

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EXAMINER

MOORE, WILLIAM W

ART UNIT	PAPER NUMBER
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1656

DATE MAILED: 12/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/500,943

Applicant(s)

POULOSE ET AL.

Examiner

William W. Moore

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 September 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3,5 and 7-10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3,5 and 7-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendment to the claims submitted 25 September 2006 should have been submitted as a separate paper as required by 37 CFR 1.4(c). The paper has been entered. However, all future correspondence must comply with 37 CFR 1.4. The amendments to the specification filed 25 September overcome the objections of record thereof and the claim amendments and claim cancellations overcome the objections of record of claims 3-6 and the rejections of record of claims herein under, second paragraph. While the amendments of claims 3 and 5 avoid the rejections of record of claims herein under 35 U.S.C. § 102, they fail to adequately address the rejections of record herein under 35 U.S.C. § 112, first paragraph, which rejections are maintained, and require a new ground of rejection under 35 U.S.C. § 103.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 5 and 7-10 remain rejected for reasons of record under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments filed 25 September 2006 have been fully considered but they are not persuasive. Although claims 1 and 2 were cancelled, the remaining polypeptide product claims 3 and 5 are still drawn to generic proteases, proteases that need not be drawn from the subgenus of subtilisin proteases, and that need not have any particular relationship to the particular subtilisin modified by Applicant wherein the particular amino acid substitutions disclosed in, e.g., Tables 3-5 of the specification are possible.

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Claims 7-10 that depend from claim 3 reach preparation of polynucleotides that encode such generic divergent proteases. Although the amended claims 3 and 5 now recite positions for correspondence to the amino acid sequence of a reference subtilisin amino acid sequence, there is no description or exemplification of the preparation of generic divergent proteases of claims 3 and 5, which may be drawn from any class of proteases, that may differ to any extent from a subtilisin protease by any number of amino acid "modifications" at positions beyond the six positions now identified by the claims. In other words, the rest of the polypeptide need not be a member of the already broad genus of subtilisin proteases. The specification does not otherwise disclose or suggest the nature or source of any serine proteases that might be modified according to the disclosure of the specification. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. § 112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The rejection of record is therefore maintained.

Claims 3, 5, and 7-10 remain rejected for reasons of record under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the modification of members of the class of serine proteases known as **subtilisins** where positions for modification can be identified by correspondence with positions in the amino acid sequence set forth in SEQ ID NO:2, does not reasonably provide enablement for modification of members of other classes serine proteases or proteases generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments filed 25 September 2006 have been fully considered but they are not persuasive. Although claims 1 and 2 were cancelled, the remaining polypeptide product claims 3 and 5 are still drawn to generic proteases, proteases that need not be drawn from the subgenus of subtilisin proteases, and that need not have any particular relationship to the particular subtilisin modified by Applicant. Claims 3 and 5 reach the

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modification of members of any class of proteases, or any class of serine proteases, by making amino acid substitutions, additions or deletions at positions beyond the six positions recited in claim 3 in any generic precursor protease and the preparation of polynucleotides encoding generic divergent proteases. Yet the specification cannot support the introduction of any number amino acid sequence alterations in the amino acid sequences of proteases generally, in any combination or any pattern, and even taken together with the prior art made of record herewith cannot identify amino acid positions in sequences of generic proteases that might be altered, nor teach the nature of the alterations to be made, even if six positions therein may be identified by some degree of correspondence with the positions in the subtilisin BPN' sequence set forth in SEQ ID NO:2. The rejection of record is therefore maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 3, 5 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over van der Osten et al. in view of Hansen et al., both of record.

Van der Osten et al., US 6,300,116 was made of record and discussed in the communication mailed 27 March 2006 for their teaching of the preparation of subtilisin variants wherein serine is substituted for arginine at a position corresponding to the subtilisin BPN' position 170 in any subtilisin, R170S, which amino acid substitution is combined, see, e.g., col. 19 at lines 3 and 14, with a substitution of a positively-charged amino acid for an uncharged amino acid, such as P129K or F189K, resulting in a subtilisin variant having the same net electrostatic charge as the precursor subtilisin protease. While van der Osten et al. also teach the subject matters of pending claims

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7-10 at columns 19-46, they do not teach the preparation of a subtilisin variant comprising any of the amino acid substitutions further to the R170S substitution now recited in the amended claim 3 or the substitution of one amino acid for another at the subtilisin correspondent position 87.

Thus the teachings of Hansen et al., US 6,605,458, made of record and discussed in the communication mailed 27 March 2006, are combined with the teachings of von der Osten et al. Hansen et al. teach that the amino acid substitution R170S may be combined in a subtilisin variant with another amino acid substitution where, "[I]n further embodiments a subtilase variant of the invention may advantageously be combined with one or more modification(s) in any of the positions: 27, 36, 57, 76, 87, 97, 101, 104, 120, 123, 167, 170, 206, 218, 222, 224, 235 and 274. Specifically the following BLS309 and BAPB92 variants are considered appropriate for combination: K27R, *36D, S57P, N76D, S87N, G97N, . . . ", reciting a list of well-known amino acid substitutions often combined with other amino acid substitutions in the prior art at col. 13, lines 3-40. As noted in the communication mailed 27 March 2006, Hansen et al. additionally teach the substitution S87N in claims 19, 41 and 68 and teach the subject matters of the pending claims 7-10 in claims 23-27, 45-50 and 72-76. It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the R170S substitution with either of the P129K or F189K substitutions of van der Osten et al., and to further combine such a paired substitution, which maintains a net absence of change of net charge in a subtilisin, and to further combine the K27R and S87N substitutions taught to be both commonplace and advantageous in the prior art in order to maintain an optimal proteolytic activity in a pH range met in most detergent compositions as admitted by the instant application and well-known to such an artisan at that time as exemplified by the teachings of the prior art of record. Such an artisan would have had

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a reasonable expectation of success in so doing because the highly alkaline *Bacillus subtilis*, such as the *Bacillus lentus* GG36 subtilisin modified by Applicant herein and the *Bacillus lentus* subtilisins PB92 and 309 modified by van der Osten et al. and Hansen et al. are often selected by those working in the art of subtilisin modification.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

William W. Moore
8 December 2006



NASHAAT T. NASHED PHD.
PRIMARY EXAMINER